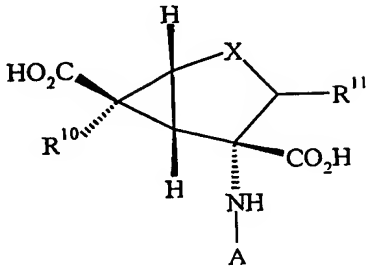
CLAIMS

1. A compound of Formula I



(I)

wherein:

A is H-$(Q)_p$-;

Q is independently selected, each time taken, from the group amino acyl;

p is an integer from 1 to 10;

X is O, S, SO, SO_2, or CR^3R^4;

R^3 is fluoro, X'OR^5, SO_3H, tetrazol-5-yl, CN, $PO_3R^6{}_2$, hydroxy, NO_2, N_3, $(CH_2)_mCOOR^{5a}$, $(CH_2)_mPO_3R^{6a}{}_2$, $NHCONHR^{5b}$, or $NHSO_2R^{5c}$ and R^4 is hydrogen; or R^3 and R^4 each represent fluoro; or R^3 and R^4 together represent =O, $=NOR^7$, $=CR^8R^9$, $=CHCOOR^{5b}$, $=CHPO_3R^{6a}{}_2$, or =CHCN; or one of R^3 or R^4 represents amino and the other represents carboxyl;

X' represents a bond, CH_2, or CO;

m is an integer from 1 to 3;

R^5, R^{5a}, R^{5b}, R^{5c}, R^7, R^8, and R^9 are independently a hydrogen atom; an optionally substituted (1-6C) alkyl group; an optionally substituted (2-6C) alkenyl group; an optionally substituted (2-6C) alkynyl group; an optionally substituted aromatic group; an optionally substituted heteroaromatic group; a non-aromatic carbocyclic group; a non-aromatic heterocyclic group; a non-aromatic monocyclic carbocyclic group fused with one or two monocyclic aromatic or heteroaromatic groups; or a non-aromatic monocyclic heterocyclic group fused with one or two monocyclic aromatic or heteroaromatic groups;

R^6 and R^{6a} independently represent hydrogen or a (1-6C)alkyl group;

R^{10} is hydrogen or fluoro; and

R^{11} is hydrogen, fluoro, or hydroxy;

or a pharmaceutically acceptable salt thereof.

2. A compound or salt according to Claim 1, provided that the compound or salt is not one in which X is CR^3R^4 wherein R^3 is fluoro and R^4 is hydrogen, p is 1, and Q is L-alanyl; or a pharmaceutically acceptable salt thereof.

3. A compound or salt according to Claim 1 or 2 wherein

A is H-$(Q)_p$-;

Q is independently selected, each time taken, from the group amino acyl;

p is an integer from 1 to 3;

X is O, S, SO, SO_2, or CR^3R^4;

R^3 is fluoro or hydroxy, and R^4 is hydrogen; or R^3 and R^4 together represent =O;

R^{10} is hydrogen or fluoro; and

R^{11} is hydrogen, fluoro, or hydroxy.

4. A compound or salt according to any one of Claims 1-3 wherein Q is an amino acyl derived from a natural amino acid.

5. A compound or salt according to any one of Claims 1-4 wherein X is SO_2.

6. A compound or salt according to any one of Claims 1-4 wherein X is CR^3R^4, R^3 is fluoro, and R^4 is hydrogen.

7. A compound or salt according to any one of Claims 1-4 wherein X is CR^3R^4, R^3 is hydroxy, and R^4 is hydrogen.

8. A pharmaceutically acceptable salt according to Claim 1 that is an acid-addition salt made with an acid which provides a pharmaceutically acceptable anion; a base-addition salt made with a base which provides a pharmaceutically acceptable anion for a compound which contains an acidic moiety; or a zwitterionic compound which contains oppositely charged groups.

9. A compound according to Claim 1 wherein

A is H-$(Q)_p$-;

Q is L-alanyl;

p is 1;

X is SO_2 or CR^3R^4;

R^3 is fluoro and R^4 is hydrogen;

R^{10} is hydrogen; and

R^{11} is hydrogen;

or the hydrochloride salt, tosylate salt, mesylate salt, esylate salt, besylate salt, or monosodium salt thereof.

10. The pharmaceutically acceptable salt according to Claim 9 which is (1*R*,4*S*,5*S*,6*S*)-4-(2'*S*-Aminopropionyl)amino]-2,2-dioxo-2λ^6-thia-bicyclo[3.1.0.]hexane-4,6-dicarboxylic acid hydrochloride or (1*R*,4*S*,5*S*,6*S*)-4-(2'*S*-2'-Aminopropionyl)amino-2,2-dioxo-2λ^6-thia-bicyclo[3.1.0.]hexane-4,6-dicarboxylic acid tosylate.

11. The compound according to Claim 1 which is (1*R*,4*S*,5*S*,6*S*)-4-(2'S-4'-methylthio-2'-aminobutanonyl)amino-2,2-dioxo-2λ^6-thia-bicyclo[3.1.0]hexane-4,6-dicarboxylic acid or a pharmaceutically acceptable salt thereof.

12. The compound according to Claim 11 which is (1*R*,4*S*,5*S*,6*S*)-4-(2'*S*-4'-methylthio-2'-aminobutanonyl)amino-2,2-dioxo-2λ^6-thia-bicyclo[3.1.0]hexane-4,6-dicarboxylic acid monohydrate.

13. The pharmaceutically acceptable salt according to Claim 1 that is 1*S*,2*S*,4*S*,5*R*,6*R*-2-(2'*S*-aminopropionyl)amino-4-hydroxy-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid hydrochloride.

14. A compound according to Claim 1 wherein

A is H-$(Q)_p$-;

Q is L-alanyl;

p is 1;

X is CR^3R^4;

R^3 is fluoro and R^4 is hydrogen;

R^{10} is hydrogen; and

R^{11} is hydrogen;

or a pharmaceutically acceptable salt thereof.

15. The compound or salt according to Claim 14 which is selected from the group consisting of:

a) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid hydrochloride;

b) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid mesylate;

c) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esylate;

d) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid besylate;

e) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid tosylate;

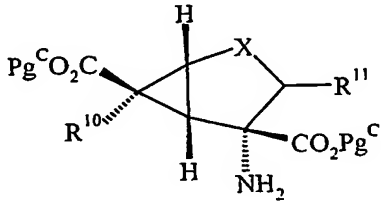
f) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid; and

g) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic monosodium salt.

16. The pharmaceutically acceptable salt according to Claim 15 which is (1R,2S,4R,5R,6R)-2-(2'*S*-2'-aminopropionyl)amino-4-fluoro-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid mesylate.

17. The pharmaceutically acceptable salt according to Claim 16 which is (1R,2S,4R,5R,6R)-2-(2'*S*-2'-aminopropionyl)amino-4-fluoro-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid mesylate monohydrate.

18. A process for preparing a compound of Formula I, or a pharmaceutically acceptable salt thereof, as claimed in Claim 1 comprising acylating a compound of formula (ii)



(ii)

with a corresponding amino acyl of Formula III

$$Pg^N\text{-}A\text{-} \qquad \text{(III)}$$

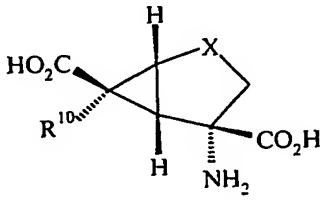
wherein Pg^N is a nitrogen-protecting group;

whereafter, for any of the above procedures, when a functional group is protected using a protecting group, removing the protecting group;

whereafter, for any of the above procedures: when a pharmaceutically acceptable salt of a compound of Formula I is required, reacting the basic form of such a compound of Formula I with an acid affording a pharmaceutically acceptable counterion; or for a compound of Formula 1 which bears an acidic moiety, reacting the acidic form of such a compound of Formula 1 with a base which affords a pharmaceutically acceptable cation; or for a zwitterionic compound of Formula 1, neutralizing the acid-addition salt form or base-addition salt form of such a compound of Formula I; or by any other conventional procedure.

19. A method for affecting the cAMP-linked metabotropic glutamate receptors in a patient, which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 1.

20. A method of administering an effective amount of a compound of Formula II,



(II)

wherein X and R^{10} are defined as in Claim 1,

which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 1.

21. A method for treating a neurological disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 1.

22. The method of Claim 21 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass and grafting; cerebral ischemia; spinal cord trauma; head trauma; Alzheimer's Disease; Huntington's Chorea; amyotrophic lateral sclerosis; AIDS-induced dementia; perinatal hypoxia; hypoglycemic neuronal damage; ocular damage and retinopathy; cognitive disorders; idiopathic and drug-induced Parkinson's Disease; muscular spasms; migraine headaches; urinary incontinence; drug tolerance, withdrawal, cessation, and craving; smoking cessation; emesis; brain edema; chronic pain; sleep disorders; convulsions; Tourette's syndrome; attention deficit disorder; and tardive dyskinesia.

23. The method of Claim 22 wherein said neurological disorder is drug tolerance, withdrawal, cessation, and craving; or smoking cessation.

24. A method for treating a psychiatric disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 1.

25. The method of Claim 24 wherein said psychiatric disorder is schizophrenia, anxiety and related disorders, depression, bipolar disorders, psychosis, and obsessive compulsive disorders.

26. The method of Claim 25 wherein said psychiatric disorder is anxiety and related disorders.

27. A pharmaceutical formulation comprising in association with a pharmaceutically acceptable carrier, dilutent or excipient, a compound of Formula I, or a pharmaceutically acceptable salt thereof.